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(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Tore DUVOLD

Application No.: NEW

Confirmation No.:

Filed: October 4, 2004

Art Unit: N/A

For: BRANCHED POLYAMINE STEROID
DERIVATIVES

Examiner: Not Yet Assigned

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

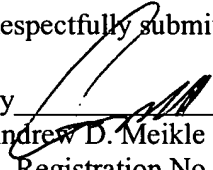
Sir:

The PTO is requested to use the amended sheets/claims attached hereto (which correspond to Article 19 amendments or to claims attached to the International Preliminary Examination Report (Article 34) during prosecution of the above-identified national phase PCT application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. for any additional fees required under 37.C.F.R. §§1.16 or 1.14; particularly, extension of time fees.

Dated: October 4, 2004
ADM/nl

Respectfully submitted,

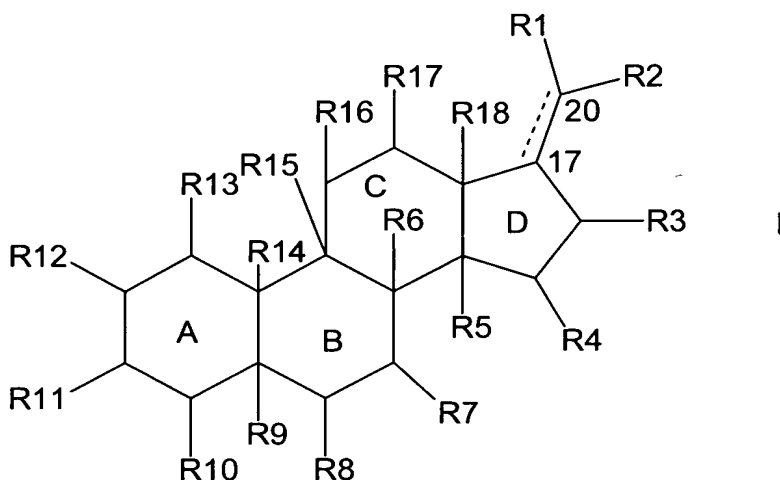
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10/509911

CLAIMS

1. A compound according to formula I



wherein the fused rings A, B, C and D are independently saturated or fully or partially unsaturated;

the bond between C-17 and C-20 is depicted with a full and a dotted line to indicate that said bond can be a single or a double bond;

wherein R1 is hydrogen, halogen, a lipophilic group, $-(Z)_n-(NR-Z)_p-N(R)_2$ or $C(O)-(Z)_n-(NR-Z)_p-N(R)_2$, wherein n is 0 or 1 and p is an integer from 1 and 5;

each Z independently represents straight or branched hydrocarbon diradical, optionally substituted with C_{1-6} alkyl, C_{1-6} alkenyl, C_{1-6} alkynyl, hydroxy, alkoxy, amino, C_{1-6} aminoalkoxy, C_{1-6} aminoalkyl, C_{1-6} aminoalkylaminocarbonyl,

C_{1-6} alkyl C_{3-8} cycloalkyl or C_{1-6} alkylheteroaryl;

each R independently represents hydrogen or C_{1-6} alkyl, C_{1-6} aminoalkyl,

C_{1-6} aminoalkoxy or C_{1-6} aminoalkylaminocarbonyl, all of which are optionally substituted with alkyl or C_{1-6} aminoalkyl;

provided that at least one Z is substituted with C_{1-6} alkyl, C_{1-6} alkenyl, C_{1-6} alkynyl, hydroxy,

alkoxy, C_{1-6} aminoalkoxy, C_{1-6} aminoalkyl, C_{1-6} aminoalkylaminocarbonyl,

C_{1-6} alkyl C_{3-8} cycloalkyl or C_{1-6} alkylheteroaryl, or at least one R is different from hydrogen;

R2 represents halogen, C_{1-4} alkyl, optionally substituted with COOH; C_{1-4} alkoxy, -COOH, $-(Z)_n-(NR-Z)_p-N(R)_2$ or $C(O)-(Z)_n-(NR-Z)_p-N(R)_2$;

R3 represents hydrogen halogen or O-R19, wherein R19 represents hydrogen, -SO₃,

C_{1-6} alkyl, C_{1-6} acyl or $-(Z)_n-(NR-Z)_p-N(R)_2$;

each of R4, R7, R8, R10, R11, R12, R13, R16 and R17 independently represent hydrogen, halogen, hydroxy, -OSO₃, -O-acyl, $-(Z)_n-(NR-Z)_p-N(R)_2$ or

$C(O)-(Z)_n-(NR-Z)_p-N(R)_2$;

each of R5, R6, R9, R14, R15 and R18 independently represent hydrogen or methyl or are each independently absent when one of the fused rings, A, B, C and D are unsaturated so as to complete the valency of the carbon atom at that site;

5 provided that at least one, and not more than three of R1, R2, R4, R7, R8, R10, R11, R12, R13, R16 and R17 is $-(Z)_n-(NR-Z)_p-N(R)_2$ or

$C(O)-(Z)_n-(NR-Z)_p-N(R)_2$;

and pharmaceutically acceptable salts or esters thereof.

10 2. A compound according to claim 1, wherein R2 represents $-(Z)_n-(NR-Z)_p-N(R)_2$ or $C(O)-(Z)_n-(NR-Z)_p-N(R)_2$.

3. A compound according to claim 1, wherein R7, R11 and/or R16 represents $-(Z)_n-(NR-Z)_p-N(R)_2$ or $C(O)-(Z)_n-(NR-Z)_p-N(R)_2$.

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4. A compound according to claim 1, wherein R1 represents a lipophilic group.

5. A compound according to claim 1, wherein R1 is selected from the group consisting of straight or branched, saturated or unsaturated C_{1-10} alkyl, aryl, C_{3-8} cycloalkyl, aralkyl with
20 1-10 carbon atoms in the alkyl moiety, C_{1-10} alkylaryl, C_{1-10} alkyl- C_{3-8} cycloalkyl, C_{1-10} alkoxy and heteroaryl.

6. A compound according to any of claims 1-5, wherein R19 represents C_{1-6} alkyl or C_{1-6} acyl.

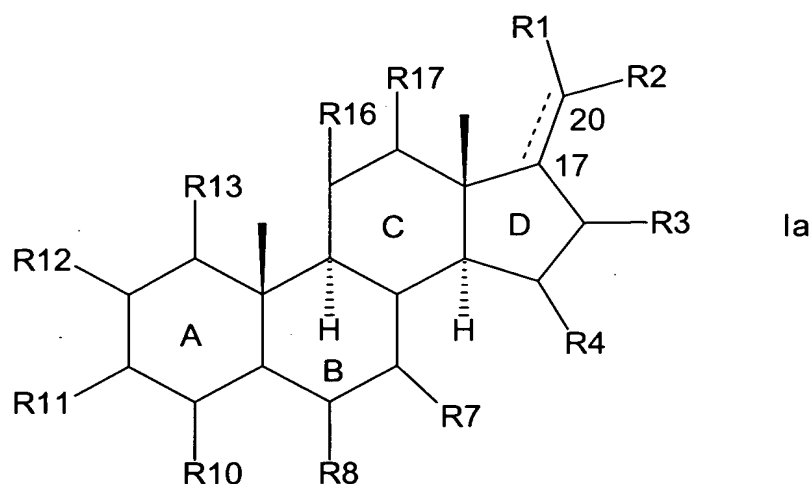
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7. A compound according to any of claims 1-6, wherein R7, R11 and/or R16 represent OH

8. A compound according to any of claims 1-5, wherein R11 represents
30 $-OSO_3$.

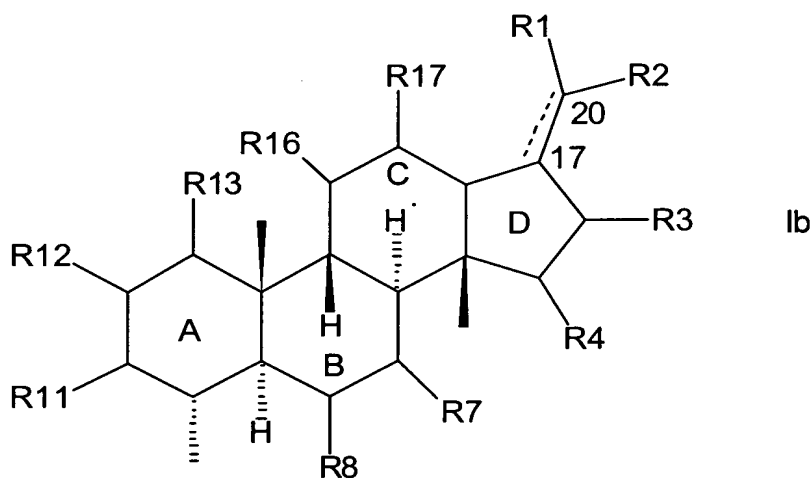
9. A compound according to any of claims 1-5, wherein R11 represents $-O$ -acyl.

35 10. A compound according to any of claims 1 which has the general formula Ia



11. A compound according to any of claims 1 which has the general formula Ib

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12. A compound according to claim 10 or 11, wherein R2 represents $-(Z)_n-(NR-Z)_p-N(R)_2$ or $C(O)-(Z)_n-(NR-Z)_p-N(R)_2$.

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13. A compound according to claim 12, wherein R7 and R11 are both hydroxy.

14. A compound according to claim 12, wherein R11 and R16 are both hydroxy.

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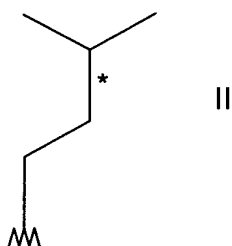
15. A compound according to claim 12, wherein R3 is $-OR_{19}$, wherein R19 is C_{1-6} alkyl or C_{1-6} acyl.

16. A compound according to claim 12, wherein R1 is a lipophilic group.

17. A compound according to claim 12, wherein R1 is a straight or branched, saturated or unsaturated C₁₋₁₀hydrocarbon.

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18. A compound according to claim 12, wherein R1 is a moiety of formula II



wherein the carbon-carbon bond denoted "*" is a single or double bond.

10 19. A compound according to claims 10 or 11, wherein R11 represents $-(Z)_n-(NR-Z)_p-N(R)_2$ or $C(O)-(Z)_n-(NR-Z)_p-N(R)_2$.

20. A compound according to claim 19, wherein R2 is C₁₋₄alkyl, optionally substituted with COOH, C₁₋₄alkoxy or COOH.

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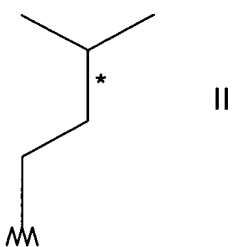
21. A compound according to claim 19, wherein R3 is O-R19, wherein R19 represents C₁₋₆alkyl or C₁₋₆acyl.

22. A compound according to claim 19, wherein R1 is a lipophilic group.

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23. A compound according to claim 19, wherein R1 is a straight or branched, saturated or unsaturated C₁₋₁₀hydrocarbon.

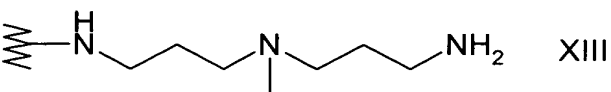
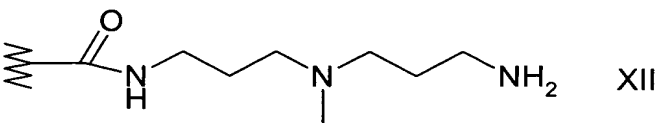
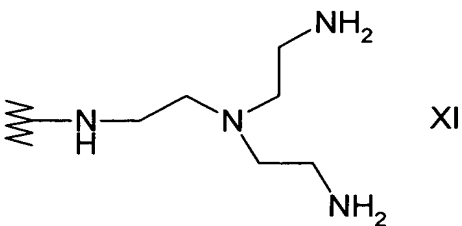
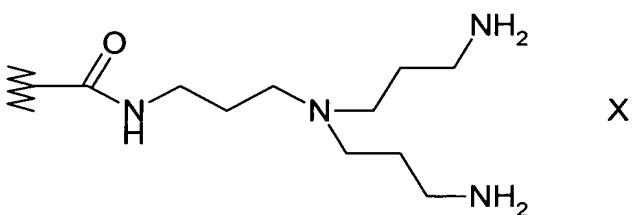
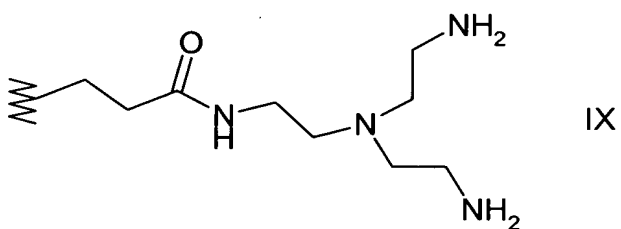
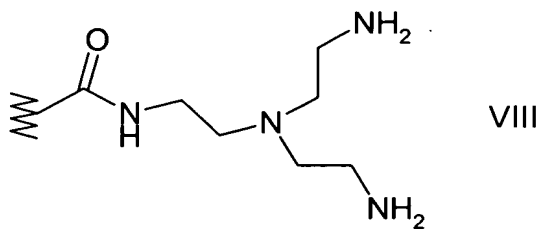
24. A compound according to claim 19, wherein R1 is a moiety of formula II

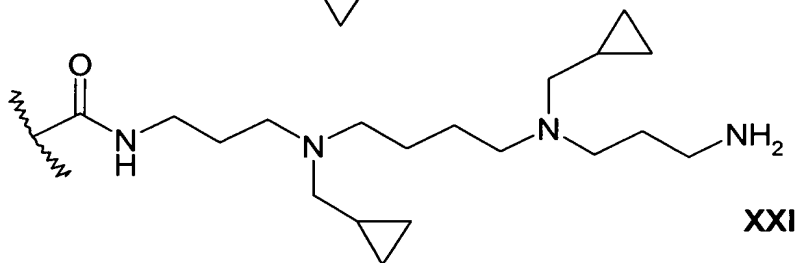
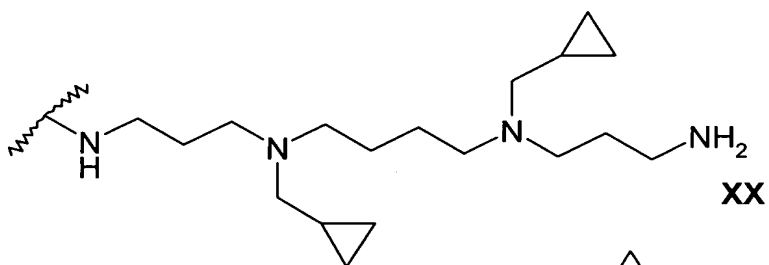
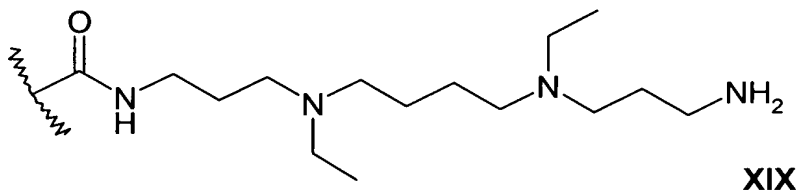
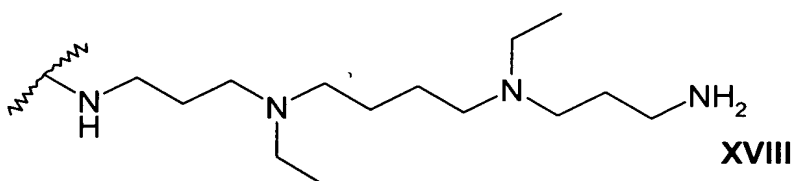
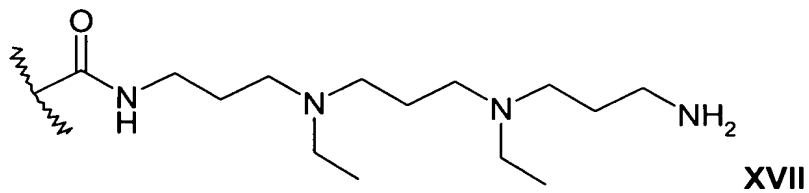
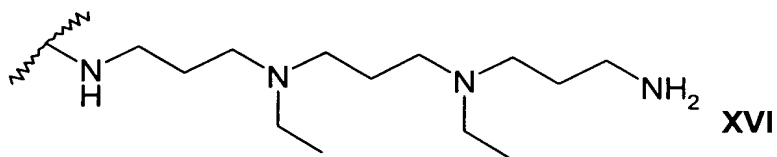


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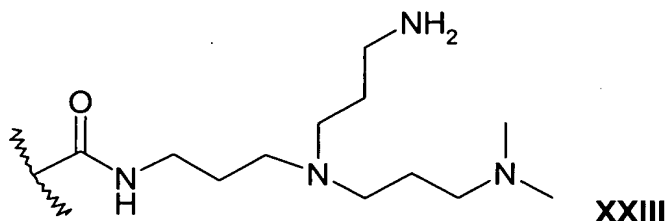
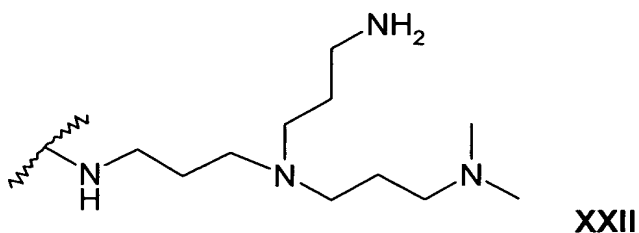
wherein the carbon-carbon bond denoted "*" is a single or double bond.

25. A compound according to any one of claims 1, 10 or 11, wherein R₂ and/or R₁₁ represents a moiety of the formula VIII, IX, X, XI, XII, XIII, XVI, XVII, XVIII, XIX, XX, XXI, XXII, XXIII





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26. A compound according to claim 1 selected from the group consisting of

- 5 21-N-{2'-[bis(2'-aminoethyl)amino]ethyl}-17R,20S,24,25-tetrahydrofusid-21-amide,
21-N-{2'-[bis(2'-aminoethyl)amino]ethyl}-11-desoxy-17R,20S,24,25-tetrahydrofusid-21-
amide,
21-N-{2'-[bis(2'-aminoethyl)amino]ethyl}-16-desacetoxy-17R,20S,24,25-tetrahydrofusid-
21-amide,
- 10 21-N-{2'-[bis(2'-aminoethyl)amino]ethyl}-13(17)-en-17,20,24,25-tetrahydrofusidan-21-
carboxamide,
21-N-{2'-[bis(2'-aminoethyl)amino]ethyl}-3 β -desacetoxy-17R,20S,24,25-tetrahydrofusid-
21-amide,
21-N-{2'-[bis(2'-aminoethyl)amino]ethyl}-9(11)-en-17R,20S,24,25-tetrahydrofusid-21-
- 15 amide,
24-N-{2'-[bis(2'-aminoethyl)amino]ethyl}-3 α -hydroxy-5 β -cholan-24-amide,
22-N-{2'-[bis(2'-aminoethyl)amino]ethyl}-23,24-bisnor-5-cholenic-22-amide,
21-N-{2'-[bis(2'-aminoethyl)amino]ethyl}-fusid-21-amide,
21-N-{3'-[bis(3'-aminopropyl)amino]propyl}-fusid-21-amide,
- 20 21-N-{2'-[bis(2'-aminoethyl)amino]ethyl}-3-OSO₃-11-desoxy-17,20,24,25-tetrahydro-
fusid-21-amide,
21-N-{2'-[bis(2'-aminoethyl)amino]ethyl}-11-desoxy-16-desacetoxy-17S,20,24,25-
tetrahydrofusid-21-amide,
21-N-{3'-[bis(3'-aminopropyl)amino]propyl}-17R,20S,24,25-tetrahydrofusid-21-amide,
- 25 22-N-{3'-[bis(3'-aminopropyl)amino]propyl}-23,24-bisnor-5-cholenic-22-amide,
21-N-{3'-[bis(3'-aminopropyl)amino]propyl}-3-OAc-17R,20S,24,25-tetrahydrofusid-21-
amide,

- 21-N-{3'-[bis(3'-aminopropyl)amino]propyl}-3-OSO₃-11-desoxy-17,20,24,25-tetrahydrofusid-21-amide,
 21-N-{3'-[bis(3'-aminopropyl)amino]propyl}-11-desoxy-16-desacetoxy-17S,20,24,25-tetrahydrofusid-21-amide,
 5 3-N-{2'-[bis(2'-aminoethyl)amino]ethyl}-fusidic acid,
 21-N-{3'-[(3'-aminopropyl)(methyl)amino]propyl}-17R,20S,24,25-tetrahydrofusid-21-amide,
 21-N-{3'-[(3'-aminopropyl)(methyl)amino]propyl}-11-desoxy-17R,20S,24,25-tetrahydrofusid-21-amide,
 10 21-N-{3'-[(3'-aminopropyl)(methyl)amino]propyl}-16-desacetoxy-17R,20S,24,25-tetrahydrofusid-21-amide,
 24-N-{3'-[(3'-aminopropyl)(methyl)amino]propyl}-3 α -hydroxy-5 β -cholan-24-amide,
 21-N-{3'-[(3'-aminopropyl)(methyl)amino]propyl}-11desoxy-16-desacetoxy-17R,20S,24,25-tetrahydrofusid-21-amide,
 15 3-N-{3'-[bis(3'-aminopropyl)amino]propyl}-fusidic acid,
 3-N-{3'-[(3'-aminopropyl)(methyl)amino]propyl}-fusidic acid,
 21-N-{3'-({4'-[(3'-amino-propyl)-methyl-amino]-butyl}-methyl-amino)-propyl}-17R,20S,24,25-tetrahydrofusid-21-amide,
 21-N-{3'-({3'-[(3'-amino-propyl)-ethyl-amino]-propyl}-ethyl-amino)-propyl}-17R,20S,24,25-tetrahydrofusid-21-amide,
 20 21-N-{3'-({4'-[(3'-amino-propyl)-ethyl-amino]-butyl}-ethyl-amino)-propyl}-17R,20S,24,25-tetrahydrofusid-21-amide,
 21-N-{3'-({3'-[(3'-amino-propyl)-ethyl-amino]-propyl}-ethyl-amino)-propyl}-11-desoxy-17R,20S,24,25-tetrahydrofusid-21-amide,
 25 21-N-{3'-({4'-[(3'-amino-propyl)-cyclopropylmethyl-amino]-butyl}-cyclopropylmethyl-amino)-propyl}-17R,20S,24,25-tetrahydrofusid-21-amide, and
 21-N-{3'-[(3'-amino-propyl)-(3'-dimethylaminopropyl)-amino]-propyl}-11-desoxy-17R,20S,24,25-tetrahydrofusid-21-amide.
- 30 27. A pharmaceutical composition comprising a compound according to any of claims 1-26 together with a pharmaceutically acceptable excipient or vehicle.
28. A composition according to claim 27 comprising another therapeutically active ingredient selected from the group consisting of penicillins, cephalosporins, tetracyclines,
 35 rifamycins, erythromycins, lincomycin, clindamycin, flouroquinolones, corticosteroids, hydrocortisone and triamcinolone.
29. The use of a compound according to any of claims 1-26 for the manufacture of a

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medicament for the treatment or prevention of infections.

30. The use according to claim 29, wherein the infection is a bacterial infection.

5 31. The use according to claim 29, wherein said compound is combined with one or more other therapeutically active ingredients.

10 32. The use according to claim 31, wherein said therapeutically active ingredient is selected from the group consisting of penicillins, cephalosporins, tetracyclines, rifamycins, erythromycins, lincomycin, clindamycin, flouroquinolones, corticosteroids, hydrocortosone and triamcinolone.

15 33. A method of preventing or treating infection, the method comprising administering to a patient in need thereof an effective amount of a compound according to any of claims 1-27.

34. A method according to claim 33, wherein said infection is a bacterial infection.

20 35. A method according to claim 33, wherein said compound is administered simultaneously or sequentially with one or more other therapeutically active ingredients.

25 36. A method according to claim 35, wherein said other therapeutically active ingredient is selected from the group consisting of penicillins, cephalosporins, tetracyclines, rifamycins, erythromycins, lincomycin, clindamycin, flouroquinolones, corticosteroids, hydrocortisone and triamcinolone.